SnapShot: Hormones of the Gastrointestinal Tract

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	Hormone	Site(s) of Production	Stimulus for Secretion	Receptor / Site of Action	Major Function(s)
STOMACH	**Gastrin**	Primarily in G cells of gastric antrum; variable extent in the duodenum; much lesser extent in colon and pancreas	Food ingestion (primarily protein)	CCK2 receptor (a GPCR) on fundic enterochromaffin-like cells and gastric parietal cells	Stimulates gastric acid secretion and epithelial cell proliferation; participates in iron homeostasis
	Ghrelin	Primarily in X/A-like (in rodents) or P/D1 (in humans) endocrine cells of the oxyntic mucosa	Fasting, before a meal	Centrally through growth hormone secretagogue receptor-1a (a GPCR) and peripherally through its receptor on vagal afferents innervating the stomach	Orexigenic effect on appetite/feeding; stimulates gastric emptying, acid secretion, and migrating motor complexes; protects against gastric stress; increases release of growth hormone
	Leptin	Chief cells and endocrine P cells in the gastric fundic region	Food ingestion, vagal nerve stimulation, CCK, and secretin	Leptin receptor Ob-R (in the gp130 family of cytokine receptors) on gastric vagal afferents and on the apical side of enterocytes along the small and large intestine	Anorexigenic effect on appetite/feeding; stimulates CCK and GLP-1 secretion; modulates intestinal absorption of nutrients
SMALL and/or LARGE INTESTINE	**Somatostatin**	Enteroendocrine D cells in the antral and fundic mucosa of the stomach and along the intestinal mucosa	Intraluminal nutrients and acid, adrenergic stimulation, CCK, and gastrin	Somatostatin receptor (rhodopsin-like GPCR, mostly the SST_2 subtype) along the GI tract and in the pancreas	Inhibits gastric acid secretion and endocrine and exocrine pancreatic secretion
	Secretin	Throughout the small intestine but primarily in enteroendocrine S cells of duodenal mucosa	Acidic chyme from stomach, digested fat and protein	Secretin receptor (family B GPCR) located on basolateral membrane of ductal and centroacinar cells of pancreas, on epithelial cells of large intrahepatic bile duct units, and in the kidney	Stimulates alkaline secretion from the pancreas (bicarbonate, water, and electrolytes) and biliary ductular systems; inhibits gastric motility and acid secretion; participates in body fluid homeostasis / osmoregulation
	GIP	Enteroendocrine K cells of the proximal small intestine (mainly duodenum)	Food ingestion (primarily carbohydrates and fat)	GIP receptor (a GPCR) on the endocrine pancreas	Acts as an incretin hormone that potentiates glucose-stimulated insulin secretion
	CCK	Enteroendocrine I cells of duodenum and jejunum	Food ingestion (primarily protein and fat)	CCK1, and perhaps CCK2 receptors (GPCRs), on vagal afferents, the stomach and upper small intestine, the pancreas and gallbladder, and in the CNS	Reduces feeding/meal size; inhibits gastric emptying and acid secretion; stimulates gall bladder contraction and pancreatic digestive enzyme secretion
	Motilin	Enteroendocrine M cells of the proximal small intestine	Interdigestive fasting period	Motilin receptor (a GPCR) on nerves and muscle of the GI tract	Induces phase III contraction of the migrating motor complex (GI motor activity)
	PYY	Enteroendocrine L cells of the jejunum, ileum, and colon	Food ingestion (primarily fat)	At least five distinct Y receptor subtypes of the GPCR family (Y1, Y2, Y4, Y5, Y6) along the GI tract, in the pancreas, and in the CNS	Reduces food intake; inhibits gastric emptying and secretion; suppresses intestinal motility and electrolyte secretion; inhibits pancreatic secretion
	GLP-1	Enteroendocrine L cells of jejunum, ileum, and colon	Food ingestion (particularly carbohydrates and fat); bile acids acting on TGR5 (a GPCR)	GLP-1 receptor (a GPCR) along the GI tract, in the endocrine pancreas, on vagal afferents, and in the CNS	Incretin effect (potentiates glucose-stimulated insulin secretion); reduces food intake; inhibits gastric emptying and GI secretion; inhibits glucagon secretion
	GLP-2	Enteroendocrine L cells of jejunum, ileum, and colon	Co-secreted with GLP-1 in response to nutrient ingestion	GLP-2 receptor (a GPCR) in the GI tract and the enteric and CNS	Stimulates cell growth in the gut mucosa and protects against apoptosis; inhibits gastric emptying and acid secretion; enhances intestinal nutrient absorption and blood flow
	OXM	Enteroendocrine L cells of jejunum, ileum, and colon	Food ingestion (particularly fat)	GLP-1 and glucagon receptors (GPCRs)	Reduces food intake; reduces gastric acid and exocrine pancreatic secretion; potentiates glucose-stimulated insulin secretion
	FGF19 (human) FGF15 (rodent)	Ileal enterocytes	Bile acids acting on FXR (a nuclear receptor)	Heteromeric receptor comprised of FGF receptor 4 (a tyrosine kinase receptor) and b-klotho (a single transmembrane co-receptor) in the liver	Suppresses bile acid synthesis; stimulates hepatic protein synthesis and glycogenesis; suppresses gluconeogenesis

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Specialized endocrine cells secrete a variety of peptide hormones all along the gastrointestinal (GI) tract, making it one of the largest endocrine organs in the body. Nutrients, hormones, and neural cues trigger the secretion of GI hormones, which act on their receptors in target tissues to facilitate the appropriate digestion, absorption, and metabolism of ingested nutrients. In addition, several GI hormones participate in the regulation of energy homeostasis through their effects on feeding behavior. Elucidation of their mechanism(s) of action has yielded several therapies for the treatment of GI disorders and metabolic diseases.

ABBREVIATIONS

GIP, glucose-dependent insulinotropic peptide or gastric inhibitory peptide; CCK, cholecystokinin; PYY, peptide YY; GLP-1, glucagon-like peptide-1; GLP-2, glucagon-like peptide-2; OXM, oxyntomodulin; FGF19, fibroblast growth factor 19.

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